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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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GOLDBERG, JEANINE ANNE

ART UNIT	PAPER NUMBER
1634	11

DATE MAILED: 07/01/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/749,998	KARUBE ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/147,791* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed April 11, 2002. Currently, claims 1-20 are pending.

Election/Restrictions

2. Applicant's election of Group I, Claims 1-20, with traverse, drawn to detection of E-coli O-157 is acknowledged.

Applicant's traverse the restriction requirement between the three methods of detecting different organisms. The response asserts that the examiner has not provided reasons or examples to support the conclusion. This argument has been thoroughly reviewed, but is found not convincing because the three methods do not require the same reagents, or method steps as previously set forth in the restriction requirement.

With respect to the assertion that there is no burden for searching the entire application, it is noted that a search for E-coli is not coextensive for the other two organisms, namely Vibrio and Salmonella. Therefore, a separate search for each of the groups is required. The response asserts that since all of the groups are classified in 435/6, there would not be a serious burden. Class 435/6 contains approximately 13,488 patents, which would be a serious burden to search.

With respect to the restriction to one primer/probe set, the examiner has deemed this requirement to be withdrawn.

Priority

3. This case claims priority to CIP application 09/147,791, filed March 1999 which is a 371 of application PCT/JP99/03077, filed July 1998.

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action.

Claim Objections

4. Claims 10, 15, 18 are objected to because the claim contains more than one period. For example, SEQ ID NO. 4 contains a period and the end of the claim contains a period. As provided in the MPEP 2422:

> (d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

This objection may be overcome by amending SEQ ID NO. 4 to read SEQ ID NO: 4 (see MPEP 608.01(m)).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-16, 18, 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-16 are indefinite over the recitation in Claim 1, "at the presence of a denaturing agent". It is unclear how one measures hybridization at the presence of a denaturing agent, or whether the claim was intended to recited "in the presence of a denaturing agent".

B) Claim 2 is indefinite over the recitation "the step of amplifying" because "the step of amplifying lacks proper antecedent basis. The rejection could be easily overcome by amending Claim 2 to delete "the step of".

C) Claims 10, 18 appear to be improper Markush group. As provided in MPEP 2173.05(h), ""wherein R is a material selected from the group consisting of A, B, C and D" is a proper limitation, then "wherein R is A, B, C or D" shall also be considered proper." Claim 10 does appear to be either of these alternatives. Therefore, amending the claims to require, a sense primer selected from the group consisting of SEQ ID NO: 4, 5, 7, 8 or 9 would be proper.

D) Claim 20 is indefinite over the recitation "the denaturing agent is formamide" because the Claim 17, from which Claim 20 depends" does not make any mention of a denaturing agent. Therefore, "the denaturing agent" lacks antecedent basis.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, 3, 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hyldig-Nielsen et al (US Pat. 5,612,458, March 1997) in view of Coull et al. (US Pat. 6,361,942, March 26, 2002).

Hyldig-Nielsen et al. (herein referred to as Hyldig-Nielsen) teaches a method for detecting a double stranded target nucleotide sequence by hybridizing a double stranded nucleotide sequence with a single stranded PNA and detecting hybridization. Hyldig-Nielsen teaches "a PNA-DNA complex can be prepared by contacting double-stranded or single-stranded DNA with a PNA molecule having a base sequence that is complementary to all or part of the DNA sequence, heating the mixture to form single-stranded molecules and allowing the mixture to cool slowly to room temperature (col. 4, lines 33-37; col 10, lines 53-60)(limitations of Claim 1). The complex may then be detected (col 10, lines 53-60)(limitations of Claim 5; 40degrees C converts to 104 degrees F). Specifically, the method described entails a complex between nucleic acid sequence and PNA may be contacted and detected with an antibody. Furthermore, the sequence may be immobilized for detection. Hyldig-Nielsen teaches that the dynamic reaction detection may be performed using a biosensor surface where the surface is plasmon resonance (SPR) detection (col. 9, lines 1-5)(limitations of Claims 3). The interaction of biomolecules with an immobilized ligand on a sensor chip is measured (col. 9, lines 15-20). Based upon the SPR detection binding will generate a signal dependent on the amount of materials bound to the surface (col. 9, lines 24-30).

Hyldig-Nielsen does not specifically teach using a denaturing agent, namely formamide in the method of detecting DNA using PNA.

Coull et al. (herein referred to as Coull) teaches "those of ordinary skill in the art of nucleic acid hybridization will recognize that factors commonly used to impose or control stringency of hybridization include formamide concentration...." (col 19, lines 14-20)(limitations of Claim 6). Coull teaches that PNA is fairly independent of ionic strength.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the method of Hyldig-Nielsen to incorporate formamide into the method to impose or control stringency of hybridization as taught by Coull. As specifically indicated by Coull the ordinary artisan would realize that formamide imposes or controls stringency of hybridization. The ordinary artisan would have desired the ability to control the stringency of the assay to meet the specificity desired.

7. Claims 1, 2, 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carlsson et al (US Pat. 6,020,126, February 2000) in view of Coull et al. (US Pat. 6,361,942, March 26, 2002).

Carlsson et al. (herein referred to as Carlsson) teaches a method for detecting a double stranded target nucleotide sequence by hybridizing a double stranded nucleotide sequence with a single stranded PNA and detecting hybridization. Carlsson teaches that the target polynucleotide region may be contained in a double-stranded polynucleotide (col. 2, lies 35-37). The method includes reacting the sample with a PAAP (generally PNA) (col. 2, lines 40-43). In the fifth embodiment of the disclosure, PNA oligomers can typically bind in a base-specific manner to a double stranded

molecule (col. 5, lines 49-53). As exemplified by Example 2, mismatches in double stranded DNA fragments amplified from human genomic DNA may be detected (col. 14, lines 50-68). Human genomic DNA was amplified from two different individuals (col. 14, lines 66-68)(limitations of Claim 2). A PNA probe was then hybridized with each of the produces and separated (col. 15, lines 6-10). The degree of hybridization was detected for the two PCR products (none in the mutant, and discrete peak in the normal) (col. 16)(limitations of Claim 7).

Carlsson does not specifically teach using a denaturing agent, namely formamide in the method of detecting DNA using PNA.

Coull et al. (herein referred to as Coull) teaches "those of ordinary skill in the art of nucleic acid hybridization will recognize that factors commonly used to impose or control stringency of hybridization include formamide concentration...." (col 19, lines 14-20). Coull teaches that PNA is fairly independent of ionic strength.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the method of Carlsson to incorporate formamide into the method to impose or control stringency of hybridization as taught by Coull. As specifically indiated by Coull the ordinary artisan would realize that formamide imposes or controls stringency of hybridization. The ordinary artisan would have desired the ability to control the stringency of the assay to meet the specificity desired.

8. Claims 3-5, are rejected under 35 U.S.C. 103(a) as being unpatentable over Carlsson et al (US Pat. 6,020,126, February 2000) in view of Coull et al. (US Pat.

6,361,942, March 26, 2002) as applied to Claims 1, 2, 6-7 above, and further in view of Wang et al. (J. Am. Chem. Soc. Vol 118, pages 7667-7670, 1996) and Jensen et al. (Biochemistry Vol 36, pages 5072-5077, 1997).

Carlsson and Coull do not specifically teach the detection of hybridization using immobilized PNA probes to detect double stranded DNA with a plasmon resonance biosensor.

However, Wang et al. (herein referred to as Wang) teaches surface-attached peptide nucleic acids (PNA) are shown to retain their unique and efficient hybridization properties, reported in solution studies. Wang teaches that DNA biosensor technology is a rapid and low cost means of detection of specific DNA sequences (page 7667, col 1). Wang teaches immobilizing PNA as the recognition layer in the DNA biosensors. Wang teaches that PNA hybrids have higher thermal stability, can be formed at low ionic strengths, permit the use of shorter probes (page 7667, col 2). Wang teaches the sue of surface-bound PNA probes provides a much greater latitude in the selection of the hybridization conditions in connection with the operation of the DNA biosensors. As seen in Table 1, dsDNA is detected using PNA probe (page 7670, col 1). Therefore, Wang teaches that PNA probes offer an efficient surface hybridization in combination with the high specificity of DNA binding (page 7670, col 2).

Moreover, Jensen et al. (herein referred to as Jensen) teaches a study of hybridization of PNA with DNA with the BIAcore technique (a surface plasmon resonance biosensor). Jensen teaches immobilizing PNA molecules upon the chip surface. Jensen teaches that the PNA surface could thereafter be regenerated by

washing with strong acid, HCL to remove all of the remaining hybridized products thereby enabling consecutive studies with the same immobilized PNA (page 5073, col 1). Jensen teaches that the technique which uses BIAcore apparatus, a surface plasmon resonance biosensor is sensitive and reproducible (page 5074, col 1). Jensen teaches the experiments were performed at 35 degrees C for all systems except for the DNA*DNA hybridization which were performed at 20 degrees C (page 5073, col 2).

Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Carlsson in view of Coull with the teachings of Wang and Jensen to make the invention as a whole. The ordinary artisan would have been motivated to have detected double stranded DNA with PNA probes on a surface plasmon resonance biosensor. Wang specifically teaches the benefits of immobilizing PNA molecules to the chip such that there is significantly higher sensitivity and specificity, faster hybridization at room and elevated temperatures, minimal dependence on ionic strength and use of shorter probes (abstract). Jensen teaches the explicit benefit of the BIAcore apparatus with PNA immobilized thereupon as being able to reuse the chip with PNA probes. Moreover, Jensen teaches that the technique which uses BIAcore apparatus, a surface plasmon resonance biosensor is sensitive and reproducible (page 5074, col 1). Therefore, combining the detection of double stranded DNA molecules using PNA on a surface plasmon resonance biosensor would have been obvious at the time the invention was made.

9. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hyldig-Nielsen et al (US Pat. 5,612,458, March 1997) in view of Coull et al. (US Pat.

6,361,942, March 26, 2002) as applied to Claims 1, 3, 5-6 above or Carlsson et al (US Pat. 6,020,126, February 2000) in view of Coull et al. (US Pat. 6,361,942, March 26, 2002) as applied to Claims 1, 2, 6 above, and further in view of Williams et al (US Pat. 6,080,400, March 2000).

Neither Hyldig-Nielsen in view of Coull or Carlsson in view of Coull specifically teaches assaying for E. coli O-157.

However, Williams teaches amplifying various subunits of the E- coli 933 genomic DNA using specific primers (col 47). Willliams also teaches E. coli is an important cause of intestinal as well as extraintestional infections. The E. coli O157:H7 serotype has gained widespread public attention in the united states due to their recently recognized association with two serious extraintestinal diseases, hemolytic uremic syndrome and thrombotic thrombocytopeni purpura (col 2). Williams teaches that O157:H7 is the predominant E. coli serotype associated with illness in N. America (col 3, lines 35-40).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the methods of Hyldig-Nielsen in view of Coull or Carlsson in view of Coull with the teachings of Williams for assaying for E. coli O-157. The ordinary artisan would have been motivated to have used the DNA/PNA detection methods to detect E. coli O-157 because E. coli O-157 is "the predominant E. coli serotype associated with illness in N. America". Moreover, the serotype is important in several serious extraintestinal diseases. Thus substation of the genomic DNA from E. coli O-

157 into the detection methods would have been obvious for the expected benefit of detecting the genomic DNA rapidly.

10. Claims 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hyldig-Nielsen et al (US Pat. 5,612,458, March 1997) in view of Coull et al. (US Pat. 6,361,942, March 26, 2002) as applied to Claims 1, 3, 5-6 above or Carlsson et al (US Pat. 6,020,126, February 2000) in view of Coull et al. (US Pat. 6,361,942, March 26, 2002) as applied to Claims 1, 2, 6 above, and further in view of Fratamico et al. (J. of Clinical Microbiology, Vol 33, No. 8, pages 2188-2191, August 1995).

Neither Hyldig-Nielsen in view of Coull or Carlsson in view of Coull specifically teaches assaying for E. coli O-157.

However, Fratamico et al. (herein referred to as Fratamico) teaches detection of E. coli O157:H7. Fratamico specifically teaches that E. coli O157:H7 is a foodborne pathogen of considerable health importance (col 1, pages 2188). Fratamio teaches using primers MK1 and MK2 which are at least 20 nucleotides in length. Fratamico's primers MK1 and MK2 contain 14 and 17 contiguous nucleotides in common with SEQ ID NO: 1, respectively.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the method of methods of Hyldig-Nielsen in view of Coull or Carlsson in view of Coull with the teachings of Fratamico for assaying for E. coli O-157. The ordinary artisan would have been motivated to have used the DNA/PNA detection methods to detect E. coli O-157 because E. coli O-157 is a foodborne pathogen of

considerable health importance. Thus substation of the genomic DNA from E. coli O-157 into the detection methods would have been obvious for the expected benefit of detecting the genomic DNA rapidly.

11. Claims 10-13, 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hyldig-Nielsen et al (US Pat. 5,612,458, March 1997) in view of Coull et al. (US Pat. 6,361,942, March 26, 2002) as applied to Claims 1, 3, 5-6 above, and further in view of Fratamico et al. (J. of Clinical Microbiology, Vol 33, No. 8, pages 2188-2191, August 1995).

Neither Hyldig-Nielsen in view of Coull specifically teaches assaying for E. coli O-157 using SEQ IDN O: 2, 4-9, 16-17.

However, Fratamico et al. (herein referred to as Fratamico) teaches detection of E. coli O157:H7. Fratamico specifically teaches that E. coli O157:H7 is a foodborne pathogen of considerable health importance (col 1, pages 2188). Fratamico teaches using primers MK1 and MK2 which are at least 20 nucleotides in length. Fratamico's primers MK1 and MK2 contain 14 and 17 contiguous nucleotides in common with SEQ ID NO: 1, respectively.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the court determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologues, however, the court stated

> "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologues because homologues often have similar properties and therefore chemists of ordinary skill

> would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed oligonucleotides simply represent functional equivalents of the MK1 and MK2 primers of Fratamico and the full length disclosed E. coli sequence concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited reference in the absence of secondary considerations. Designing primers based upon a know sequence to obtain functional equivalents which would amplify the known sequence a easily obtained by the ordinary artisan. Therefore, SEQ ID NO: 4, 5, 7, 8, 9 and 6 which are found within the known E. coli sequence are obvious. Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the method of methods of Hyldig-Nielsen in view of Coull with the teachings of Fratamico for assaying for E. coli O-157. The ordinary artisan would have been motivated to have used the DNA/PNA detection methods to detect E. coli O-157 because E. coli O-157 is a foodborne pathogen of considerable health importance. Thus substation of the genomic DNA from E. coli O-157 into the detection methods would have been obvious for the expected benefit of detecting the genomic DNA rapidly.

12. Claims 10-11, 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carlsson et al (US Pat. 6,020,126, February 2000) in view of Coull et al. (US Pat. 6,361,942, March 26, 2002) as applied to Claims 1, 2, 6 above, and further in view of

Fratamico et al. (J. of Clinical Microbiology, Vol 33, No. 8, pages 2188-2191, August 1995) and Takeda (JP 1992297488-A 1, October 1992).

Neither Hyldig-Nielsen in view of Coull specifically teaches assaying for E. coli O-157 using SEQ ID NO: 2, 4-9, 16-17.

However, Fratamico et al. (herein referred to as Fratamico) teaches detection of E. coli O157:H7. Fratamico specifically teaches that E. coli O157:H7 is a foodborne pathogen of considerable health importance (col 1, pages 2188). Fratamico teaches using primers MK1 and MK2 which are at least 20 nucleotides in length. Fratamico's primers MK1 and MK2 contain 14 and 17 contiguous nucleotides in common with SEQ ID NO: 1, respectively.

Moreover, Takeda teaches an alignment of VT2 and several other strains of E. coli.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the court determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologues, however, the court stated

> "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologues because homologues often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed oligonucleotides simply represent functional equivalents of the MK1 and MK2 primers of Fratamico and the full length disclosed E. coli sequence of Takeda concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie*

obvious over the cited reference in the absence of secondary considerations. Designing primers based upon a know sequence to obtain functional equivalents which would amplify the known sequence a easily obtained by the ordinary artisan. Therefore, SEQ ID NO: 4, 5, 7, 8, 9 and 6 which are found within the known E. coli sequence are obvious. Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the method of methods of Hyldig-Nielsen in view of Coull with the teachings of Fratamico and Takeda for assaying for E. coli O-157. The ordinary artisan would have been motivated to have used the DNA/PNA detection methods to detect E. coli O-157 because E. coli O-157 is a foodborne pathogen of considerable health importance. Thus substation of the genomic DNA from E. coli O-157 into the detection methods would have been obvious for the expected benefit of detecting the genomic DNA rapidly.

13. Claims 3-5, are rejected under 35 U.S.C. 103(a) as being unpatentable over Carlsson et al (US Pat. 6,020,126, February 2000) in view of Coull et al. (US Pat. 6,361,942, March 26, 2002), and further in view of Wang et al. (J. Am. Chem. Soc. Vol 118, pages 7667-7670, 1996) and Jensen et al. (Biochemistry Vol 36, pages 5072-5077, 1997 as applied to Claims 3-5 above, and further in view of Fratamico et al. (J. of Clinical Microbiology, Vol 33, No. 8, pages 2188-2191, August 1995).

Carlsson, Coull, Wang and Jenson do not specifically teach assaying for E. coli O-157 using SEQ ID NO: 2, 4-9, 16-17.

However, Fratamico et al. (herein referred to as Fratamico) teaches detection of E. coli O157:H7. Fratamico specifically teaches that E. coli O157:H7 is a foodborne pathogen of considerable health importance (col 1, pages 2188). Fratamico teaches using primers MK1 and MK2 which are at least 20 nucleotides in length. Fratamico's primers MK1 and MK2 contain 14 and 17 contiguous nucleotides in common with SEQ ID NO: 1, respectively.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the court determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologues, however, the court stated

> "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologues because homologues often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed oligonucleotides simply represent functional equivalents of the MK1 and MK2 primers of Fratamico and the full length disclosed E. coli sequence concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited reference in the absence of secondary considerations. Designing primers based upon a know sequence to obtain functional equivalents which would amplify the known sequence a easily obtained by the ordinary artisan. Therefore, SEQ ID NO: 4, 5, 7, 8, 9 and 6 which are found within the known E. coli sequence are obvious. Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the method of method of Carlsson, Coull, Wang and Jenson

with the teachings of Fratamico for assaying for E. coli O-157. The ordinary artisan would have been motivated to have used the DNA/PNA detection methods to detect E. coli O-157 because E. coli O-157 is a foodborne pathogen of considerable health importance. Thus substation of the genomic DNA from E. coli O-157 into the detection methods would have been obvious for the expected benefit of detecting the genomic DNA rapidly.

Conclusion

14. No claims allowable over the art.

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A) Drewe et al. WO00/05408 teaches a method of nucleic acid detection using triple helix formation with PNA. The detection is effected using a surface plasmon resonance detector.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of formal matters can be directed to the patent analyst, Pauline Farrier, whose telephone number is (703) 305-3550.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg

Jeanine Goldberg
June 26, 2002